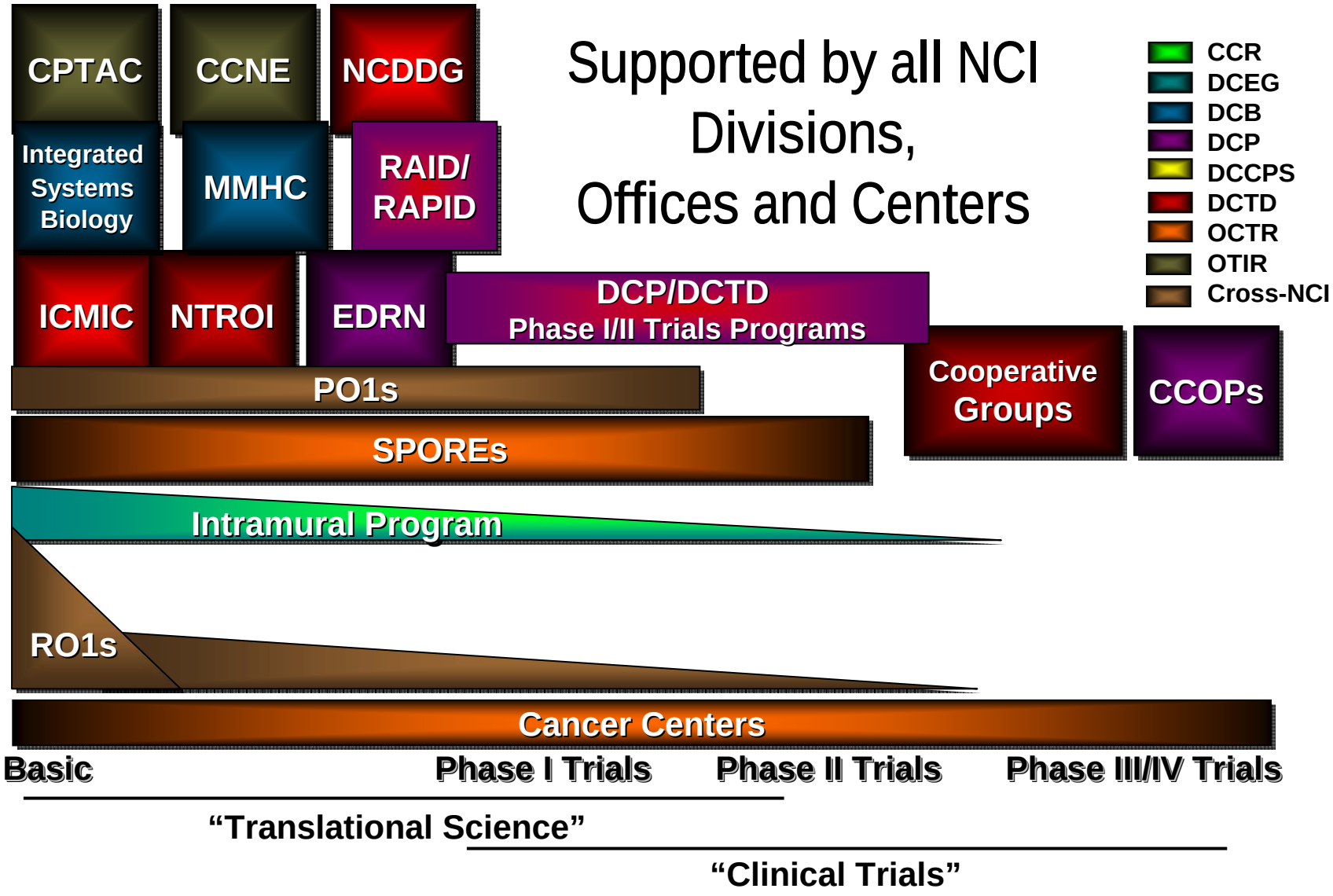
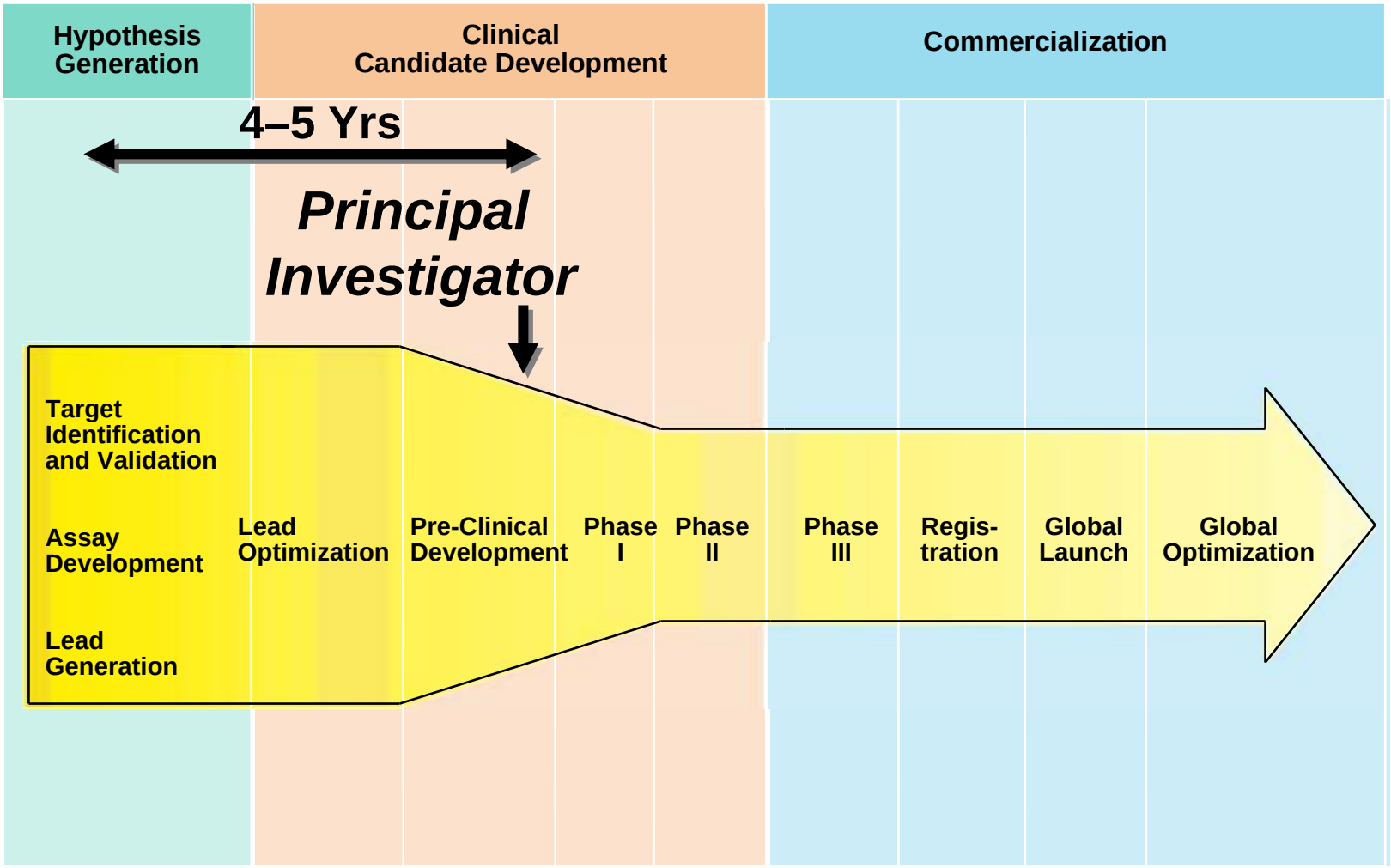
Translational Research Interface with the NCI-Supported Clinical Trials System

James H. Doroshow, M.D.
Division of Cancer Treatment and Diagnosis
National Cancer Institute

November 7, 2008

Current Infrastructure and Funding Mechanisms





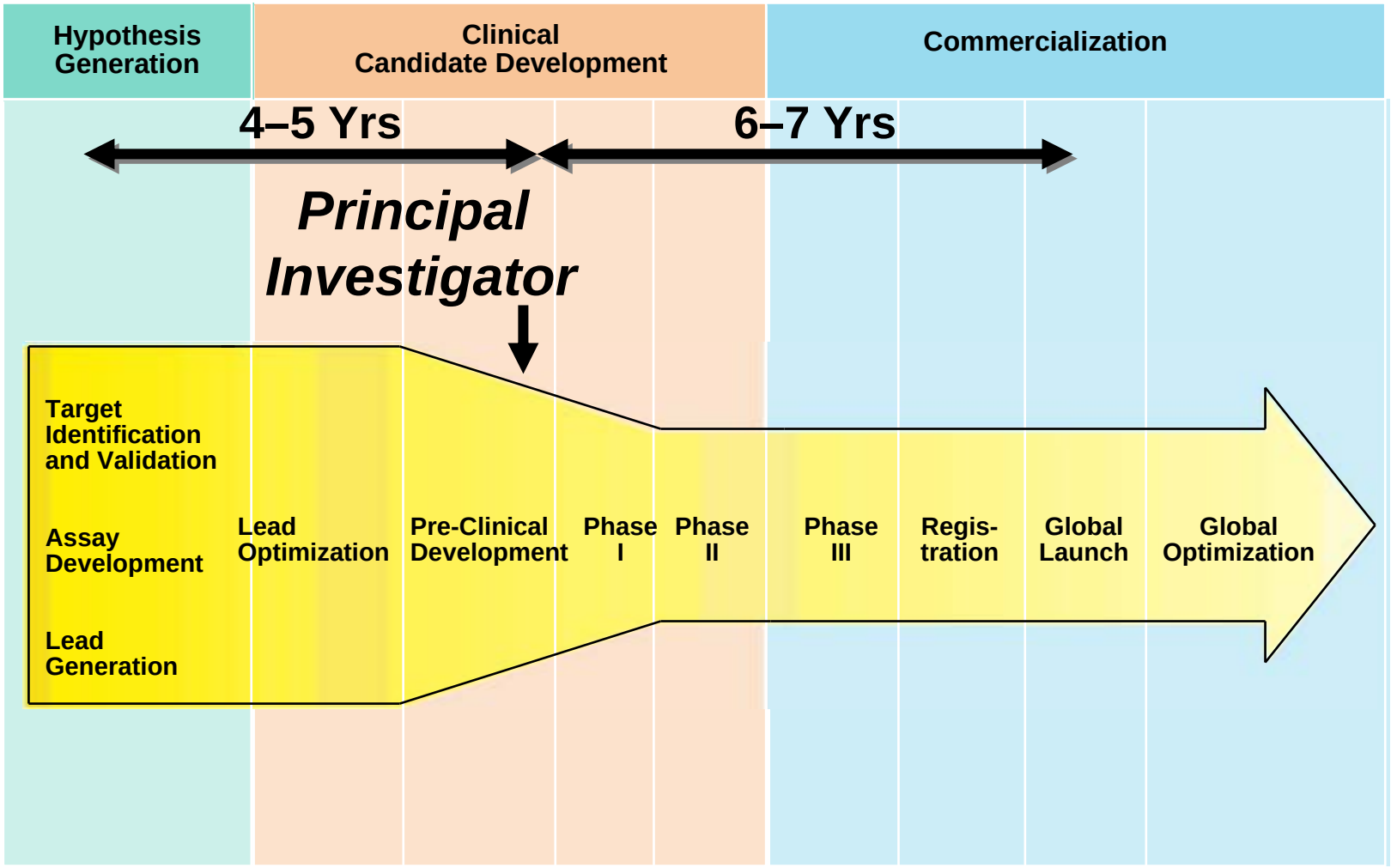
Drug/Biological Development Time Course: 10–12 Years

NCI TRANSLATES

NCI Translational Science Meeting

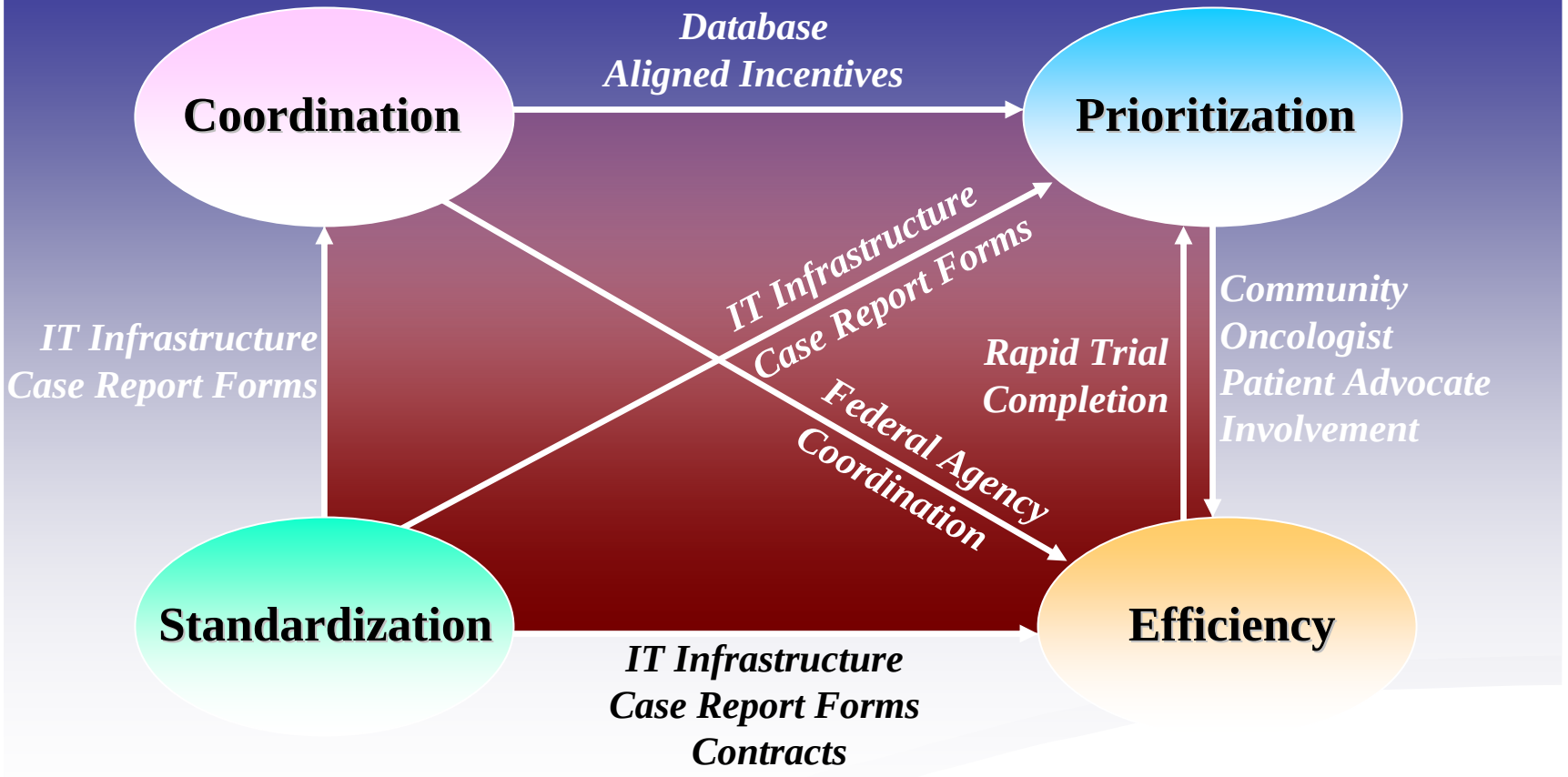
CROSSING THE VALLEY OF DEATH

A chasm has opened up between biomedical researchers and the patients who need their discoveries. **Declan Butler** asks how the ground shifted and whether the US National Institutes of Health can bridge the gap.



Drug/Biological Development Time Course: 10–12 Years

NCI Clinical Research Management
Implementation of CTWG Initiatives



Prioritization & Scientific Quality

- **Phase I: Inv. Drug Steering Cmte.**
  - **Novel approaches to phase 2 design**
  - **Cardiovascular toxicities of targeted rx's**
  - **Review of NCI IND drug solicitations**
  - **Strategic input to NCI drug portfolio**

- **Disease-based Scientific Steering Cmte.'s for phase III/large phase II concept review; brings together Coop Grp, SPORE, PO1, CCOP, RO1 trialists/translational investigators; clinical trial sots**
  - **GI, GYN, H&N, Symptom Management**
  - **GU, Lung, Pt. Advocates 2008**
  - **Breast, Heme 2009**

Prioritization & Scientific Quality

- **Developed mechanism to support Coop Grps and CCOP Research bases so that critical biomarker and quality of life studies integral to national phase III clinical trials could be pursued: $5M in 2008**
- **Developed assay standardization criteria for use in prioritization of requests for these funds**
- **Developed evaluation criteria for prioritization of essential symptom management and quality of life studies**

Standardization

- **Remote data capture system for Coop Grp trials: Distribute to all NCI-supported Clinical Trials Sites**
- **eCRF Initiative**
- **Standard Clinical Trials Agreement Clauses**

STANDARDIZED CLINICAL TRIAL AGREEMENTS

- Identify key clauses that delay or complicate negotiations
- Determine if perception is correct that negotiations lead to consistent key concepts for those clauses
- Draft proposed language for common key concepts identified
- Obtain input from participants on language

- **Involved legal and business representatives from participants**
  - **17 reps. from LSC companies**
  - **26 reps. from NCI-Designated Cancer Centers**
- **Obtained copies of 78 clinical trial agreements from participating organizations**
  - **49 redacted copies of final negotiated agreements**
  - **29 agreement templates**
    - **Approximately equal numbers of agreements from LSC companies and Cancer Centers**
    - **Agreements included company-sponsored and investigator-initiated trials**

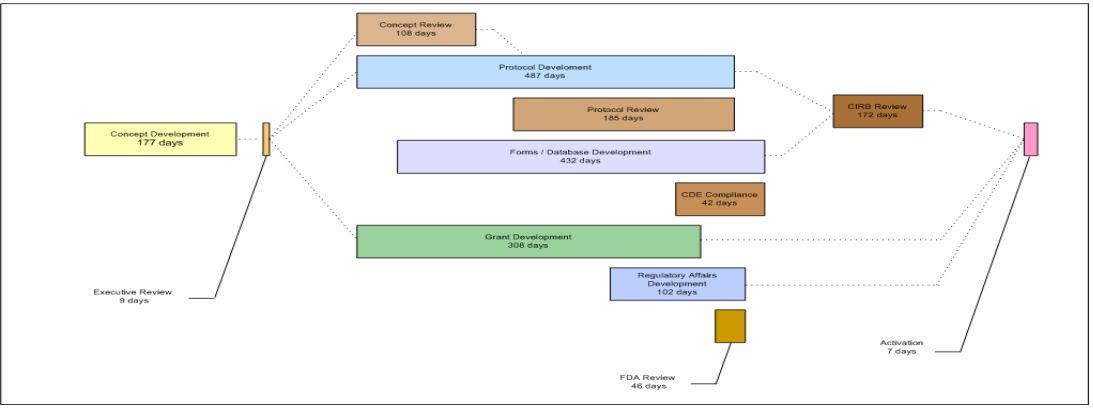
- Identified 45 key concepts in the 7 clause categories
- Captured exact language that embodied these concepts for all 78 agreements
- Organized agreement language into categories representing embodied concept
- Analyzed results for similarities and differences in key concepts across final negotiated agreements
- Analyzed template agreements for key differences with negotiated agreements

- **Final negotiated agreements showed greater than 67% convergence on the vast majority of concepts analyzed**
- **Drafted proposed clauses based on common concepts identified**
- **Obtained input on proposed clauses from legal and business participants**
- **Refined proposed clauses based on feedback**

OBTAINED favorable Business Review Letter from Dept. of Justice 9/17/08: Project reviewed; no intention to challenge initiative

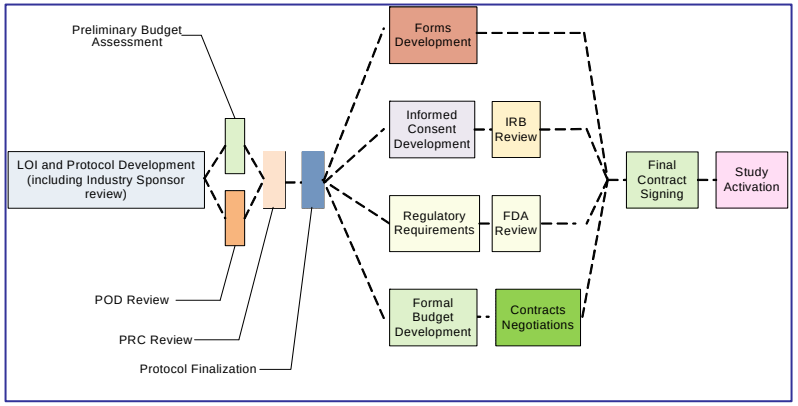
Opening a Cooperative Group Study

Cooperative Group Processes



Median: 784 to 808 days*
Range: 435-1604 days

Comprehensive Cancer Center Processes



Median: 116 to 252 days*
Range: 21-836 days

* Depending Upon Site, based on the Phase III trials studied

Efficiency

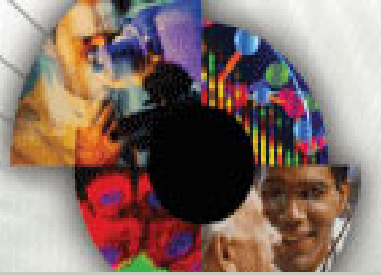
- **Completed management analysis of clinical trials activation timelines at Coop Groups, Cancer Centers, and CTEP: Operational Efficiency Working Group actively developing approaches to cutting timelines in half**

- **Developed clinical trial complexity models: provided additional support for rapid completion of difficult phase III studies and studies for underserved populations**

Coordination

- **Develop a comprehensive database of NCI-supported clinical trials: Pilot near completion at Dana-Farber, Northwestern, St. Jude, and Wake Forrest; full operation in 2009**
- **Develop mechanism to support multisite translational clinical trials in rare diseases and areas not currently a major focus for Coop Groups: Pilot studies from H&N SSC and H&N SPORES initial focus utilizing the NCI's CTSU**
- **Guideline harmonization: CCSG, SPORE, and Cooperative Groups**

TRWG/CTWG Interface



Basic Science Discovery

- Promising molecule or gene target
- Candidate protein biomarker
- Basic epidemiologic finding

Early Translation

- Partnerships & collaboration (academia, government, industry)
- Intervention development*
- Phase I/II trials

Late Translation

- Phase III trials
- Regulatory
- Partnerships
- Production & commercialization
- Phase IV trials – approval for additional uses

Dissemination

- To community health providers
- To patients & public

Adoption

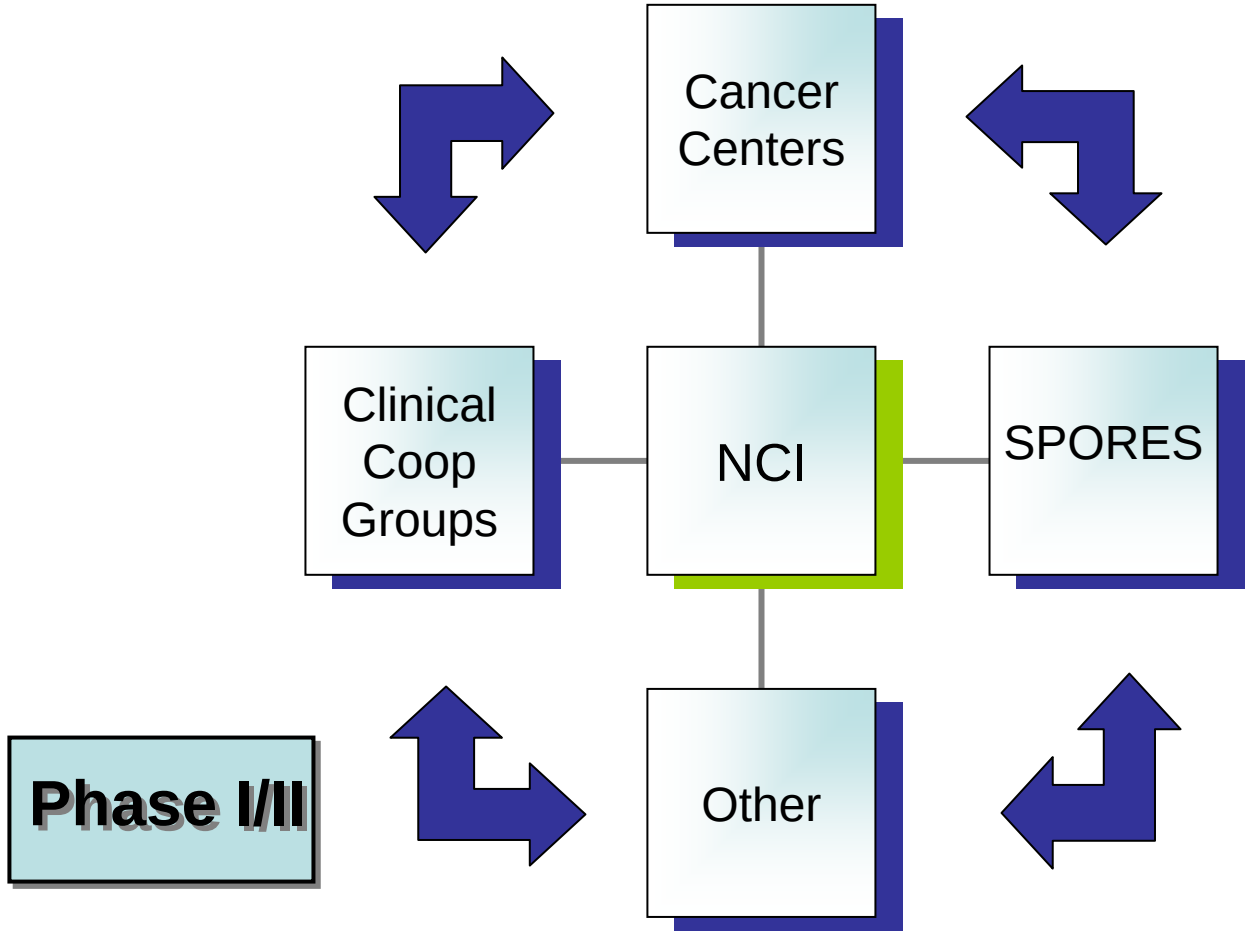
- Adoption of advance by providers, patients, public
- Payment mechanism(s) in place to enable adoption

**New drug, assay, device, behavioral intervention, educational materials, training*

Focus of TRWG

TRWG/CTWG Interface

President's Cancer Panel, 2004-2005 Annual Report

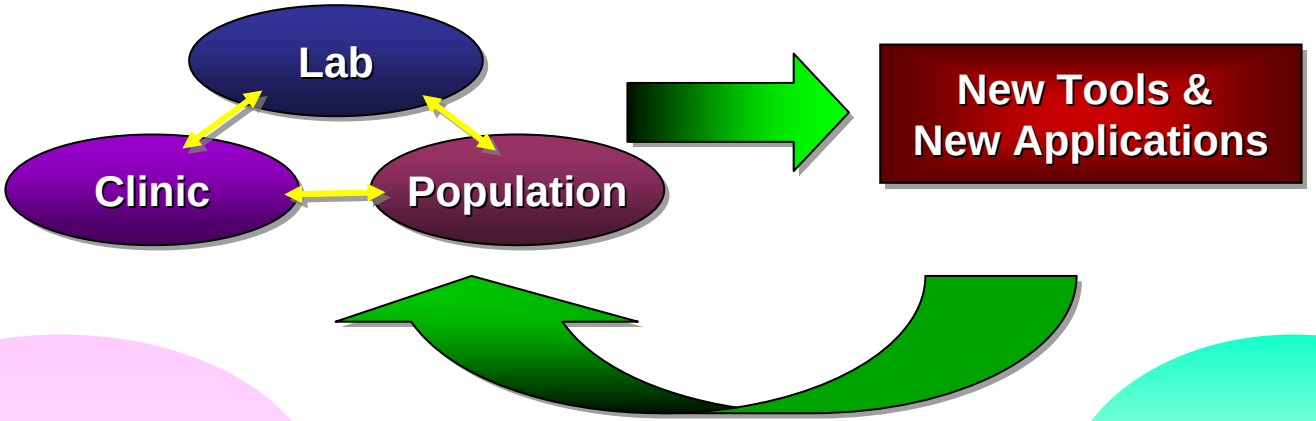

Cancer Centers
Clinical Coop Groups
NCI
SPORES
Other
Phase I/II

NCI TRANSLATES

NCI Translational Science Meeting

Prioritization & Scientific Quality

Efficiency



Coordination

Standardization